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USPT,PGPB,JPAB,EPAB,DWPI	((Dumoutier J\$)[IN] AND (renauld)[IN]) and TIF\$	1	<u>L3</u>
USPT,PGPB,JPAB,EPAB,DWPI	(Dumoutier J\$)[IN] AND (renauld)[IN]	26	<u>L2</u>
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=> s dumoutier L?/au or renauld J?/au  
L1 365 DUMOUTIER L?/AU OR RENAULD J?/AU

=> s l1 and TIF?  
L2 12 L1 AND TIF?

=> dup rem l2  
PROCESSING COMPLETED FOR L2  
L3 6 DUP REM L2 (6 DUPLICATES REMOVED)

=> dis l3 1-6 ibib abs

L3 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2001 ACS  
ACCESSION NUMBER: 2000:291060 CAPLUS  
DOCUMENT NUMBER: 132:333389  
TITLE: Isolated nucleic acid molecules which encode T cell  
inducible factors (TIFs), the proteins  
encoded, and uses thereof  
INVENTOR(S): Dumoutier, Laure; Louhed, Jamila;  
Renauld, Jean-christophe  
PATENT ASSIGNEE(S): Ludwig Institute for Cancer Research, USA  
SOURCE: PCT Int. Appl., 46 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000024758	A1	20000504	WO 1999-US24424	19991018
W:	AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, BG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, T2, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
AU 9965206	A1	20000515	AU 1999-65206	19991018
PRIORITY APPLN. INFO.:			US 1998-178973 A	19981026
			US 1999-354243 A	19990716
			WO 1999-US24424 W	19991018
AB	The invention involves isolation of nucleic acid mols. encoding TIFs, the expression of the TIFs which are upregulated by interleukin-9. The amino acid sequences of the TIF proteins			

which correspond to the nucleic acid molecules show some structural features of cytokines. In addn. to the nucleic acid mols. and the TIF proteins, use of the mols. for detg. effectiveness of interleukin 9, for stimulating STAT protein, for inhibiting activation of STAT protein are disclosed. Also provided are TIF inhibitor comprising antibodies and antisense mols. TIF mutein is useful for alleviating asthma or allergy.

#### REFERENCE COUNT:

#### REFERENCE(S):

- (1) Demoulin; Journal of Biological Chemistry 1999, V274(36), P25855 CAPLUS
- (2) Demoulin; Molecular and Cellular Biology 1996, V16(9), P4710 CAPLUS
- (3) Levitt; US 5908839 A 1999 CAPLUS
- (4) Seidel; US 5814517 A 1998 CAPLUS
- (5) Zhu; Journal of Biological Chemistry 1997, V272(34), P21334 CAPLUS

#### L3 ANSWER 2 OF 6

ACCESSION NUMBER: 2000474382 MEDLINE DUPLICATE 1  
 DOCUMENT NUMBER: 20420346 PubMed ID: 10954742  
 TITLE: Human interleukin-10-related T cell-derived inducible factor: molecular cloning and functional characterization as an hepatocyte-stimulating factor.  
 AUTHOR: Dumoutier L; Van Roost E; Colau D; Renauld J  
 CORPORATE SOURCE: Ludwig Institute for Cancer Research, Brussels Branch and the Experimental Medicine Unit, Christian de Duve Institute of Cellular Pathology, Universite Catholique de Louvain, Avenue Hippocrate 74, B1200-Brussels, Belgium.  
 SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (2000 Aug 29) 97 (18) 10144-9. Journal code: PV3; 7505876. ISSN: 0027-8424.  
 PUB. COUNTRY: United States  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 OTHER SOURCE: GENBANK-AJ277247  
 ENTRY MONTH: 200010  
 ENTRY DATE: Entered STN: 20001012  
 Last Updated on STN: 20001012  
 Entered Medline: 20001005

AB IL-10-related T cell-derived inducible factor (IL-TIF or IL-21) is a new cytokine structurally related to IL-10 and originally identified in the mouse as a gene induced by IL-9 in T cells and mast cells. Here, we report the cloning of the human IL-TIF cDNA, which shares 79% amino acid identity with mouse IL-TIF and 25% identity with human IL-10. Recombinant human IL-TIF was found to activate signal transducer and activator of transcription factors-1 and -3 in several hepatoma cell lines. IL-TIF stimulation of HepG2 human hepatoma cells up-regulated the production of acute phase reactants such as serum amyloid A, alpha1-antichymotrypsin, and haptoglobin. Although IL-10 and IL-TIF have distinct activities, antibodies directed against the beta chain of the IL-10 receptor blocked the induction of acute phase reactants by IL-TIF, indicating that this chain is a common component of the IL-10 and IL-TIF receptors. Similar acute phase reactant induction was observed in mouse liver upon IL-TIF injection, and IL-TIF expression was found to be rapidly increased after lipopolysaccharide (LPS) injection, suggesting that this cytokine contributes to the inflammatory response in vivo.

#### L3 ANSWER 3 OF 6

ACCESSION NUMBER: 2000126044 MEDLINE DUPLICATE 2  
 DOCUMENT NUMBER: 20126044 PubMed ID: 10657629  
 TITLE: Cloning and characterization of IL-10-related T cell-derived inducible factor (IL-TIF), a novel cytokine structurally related to IL-10 and inducible by IL-9.  
 AUTHOR: Dumoutier L; Louahed J; Renauld J C  
 CORPORATE SOURCE: Ludwig Institute for Cancer Research, Brussels, Belgium.  
 SOURCE: JOURNAL OF IMMUNOLOGY, (2000 Feb 15) 164 (4) 1814-9. Journal code: IFB; 2985117R. ISSN: 0022-1767.  
 PUB. COUNTRY: United States  
 LANGUAGE: English  
 FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals  
 OTHER SOURCE: GENBANK-AJ249491; GENBANK-AJ249492  
 ENTRY MONTH: 200003  
 ENTRY DATE: Entered STN: 20000320  
 Last Updated on STN: 20000320  
 Entered Medline: 20000309

AB IL-9 is a Th2 cytokine active on various cell types such as T and B lymphocytes, mast cells, and eosinophils, and potentially involved in allergy and asthma. To understand better the molecular mechanisms underlying the activity of this cytokine, we used a cDNA subtraction method to identify genes specifically induced by IL-9 in mouse T cells. One of the IL-9-regulated genes isolated by this approach turned out to encode a 180-amino acid long protein, including a potential signal peptide, and showing 22% amino acid identity with IL-10. This protein, designated IL-10-related T cell-derived inducible factor (IL-TIF), is induced by IL-9 in thymic lymphomas, T cells, and mast cells, and by lectins in freshly isolated splenocytes. Experiments concerning the mechanism regulating IL-TIF expression in T cells indicate that IL-9 induction is rapid (within 1 h), does not require protein synthesis, and depends on the activation of the Janus kinase (JAK)-STAT pathway. In vivo, constitutive expression of IL-TIF was detected by RT-PCR in thymus and brain, suggesting that the role of this new factor is not restricted to the immune system. Transfection of HEK293 cells with the IL-TIF cDNA resulted in the production of a glycosylated protein of about 25 kDa that was found to induce STAT activation in mesangial and neuronal cell lines. Further studies will have to address the possibility that some of the IL-9 activities may be mediated by IL-TIF.

#### L3 ANSWER 4 OF 6

ACCESSION NUMBER: 2001223439 MEDLINE DUPLICATE 3  
 DOCUMENT NUMBER: 21069354 PubMed ID: 11197690  
 TITLE: IL-TIF/IL-22: genomic organization and mapping of the human and mouse genes.  
 AUTHOR: Dumoutier L; Van Roost E; Amey G; Michaux L; Renauld J C  
 CORPORATE SOURCE: Ludwig Institute for Cancer Research, Brussels Branch, Experimental Medicine Unit, Christian de Duve Institute of Cellular Pathology, Brussels, Belgium.  
 SOURCE: GENES AND IMMUNITY, (2000 Dec) 1 (8) 488-94.

PUB. COUNTRY: Journal code: DXO; 10095 ISSN: 1466-4879.  
England: United Kingdom  
Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200104  
ENTRY DATE: Entered STN: 20010502  
Last Updated on STN: 20010502  
Entered Medline: 20010426

AB IL-TIF is a new cytokine originally identified as a gene induced by IL-9 in murine T lymphocytes, and showing 22% amino acid identity with IL-10. Here, we report the sequence and organization of the mouse and human IL-TIF genes, which both consist of 6 exons spreading over approximately 6 Kb. The IL-TIF gene is a single copy gene in humans, and is located on chromosome 12q15, at 90 Kb from the IFN gamma gene, and at 27 Kb from the AK155 gene, which codes for another IL-10-related cytokine. In the mouse, the IL-TIF gene is located on chromosome 10, also in the same region as the IFN gamma gene. Although it is a single copy gene in BALB/c and DBA/2 mice, the IL-TIF gene is duplicated in other strains such as C57Bl/6, FVB and 129. The two copies, which show 98% nucleotide identity in the coding region, were named IL-TIF alpha and IL-TIF beta. Beside single nucleotide variations, they differ by a 658 nucleotide deletion in IL-TIF beta, including the first non-coding exon and 603 nucleotides from the promoter. A DNA fragment corresponding to this deletion was sufficient to confer IL-9-regulated expression of a luciferase reporter plasmid, suggesting that the IL-TIF beta gene is either differentially regulated, or not expressed at all.

L3 ANSWER 5 OF 6 BIOSIS COPYRIGHT 2001 BIOSIS  
ACCESSION NUMBER: 2000:468282 BIOSIS  
DOCUMENT NUMBER: PREV200000468282  
TITLE: IL-TIF induces acute phase reactant production by hepatocytes through IL-10Rbeta.  
AUTHOR(S): Dumoutier, L. (1); Van Roost, E. (1); Colau, D. (1); Renault, J.-C. (1)  
CORPORATE SOURCE: (1) Brussels Branch, Ludwig Institute for Cancer Research, Brussels Belgium  
SOURCE: Immunology Letters, (September, 2000) Vol. 73, No. 2-3, pp. 261. print.  
Meeting Info.: 24th European Immunology Meeting of the European Federation of Immunological Societies (EFIS) Poznan, Poland September 23-26, 2000 European Federation of Immunological Societies  
. ISSN: 0165-2478.  
DOCUMENT TYPE: Conference  
LANGUAGE: English  
SUMMARY LANGUAGE: English

L3 ANSWER 6 OF 6 BIOSIS COPYRIGHT 2001 BIOSIS  
ACCESSION NUMBER: 2000:467485 BIOSIS  
DOCUMENT NUMBER: PREV200000467485  
TITLE: Cloning and characterization of mouse and human TIF, a new IL-1-related cytokine.  
AUTHOR(S): Dumoutier, L. (1); Ameye, G. (1); Michaux, L. (1); Renault, J.-C. (1)  
CORPORATE SOURCE: (1) Ludwig Institute for Cancer Research, Brussels Branch, Cliniques Univesitaires St-Luc, B-1200, Brussels Belgium  
SOURCE: Cytokine, (Nov., 1999) Vol. 11, No. 11, pp. 969. print.  
Meeting Info.: Seventh Annual Conference of the International Cytokine Society Hilton Head, South Carolina, USA December 5-9, 1999 The International Cytokine Society  
. ISSN: 1043-4666.  
DOCUMENT TYPE: Conference  
LANGUAGE: English  
SUMMARY LANGUAGE: English

=> s ILTif  
L4 1 ILTIF  
=> s IL-TIF  
L5 15 IL-TIF

=> dup rem 15  
PROCESSING COMPLETED FOR L5  
L6 7 DUP REM L5 (8 DUPLICATES REMOVED)

=> dis 16 1-7 ibib abs kwic

L6 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2001 ACS  
ACCESSION NUMBER: 2001:417148 CAPLUS  
DOCUMENT NUMBER: 135:32751  
TITLE: Protein and cDNA sequences encoding human cytokine receptor Zcytor16 and its therapeutic and diagnostic uses  
INVENTOR(S): Presnell, Scott R.; Xu, Wenfeng; Kindsvogel, Wayne; Chen, Zhi  
PATENT ASSIGNEE(S): Zymogenetics, Inc., USA  
SOURCE: PCT Int. Appl., 210 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001040467	A1	20010607	WO 2000-US32703	20001201
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
PRIORITY APPLN. INFO.:			US 1999-169049 P 19991203	
			US 2000-232219 P 20000913	
			US 2000-244610 P 20001031	

AB This present invention provides protein and cDNA sequences encoding human cytokine receptor Zcytor16. The cytokine receptor Zcytor16 is expressed

in lymphoid, placenta, spleen, tonsil and its gene has been mapped to human chromosome 6 (6q24.1-25.2). Cytokine receptor Zcytor16 is a class II cytokine receptor and its binding to human IL-TIF could inhibit the proliferation and differentiation of hematopoietic cells. This invention also provide the test kit to detect genetic abnormality and cancer in patients.

# REFERENCE COUNT:

REFERENCE(S):

AB This present invention provides protein and cDNA sequences encoding human cytokine receptor Zcytor16. The cytokine receptor Zcytor16 is expressed in lymphoid, placenta, spleen, tonsil and its gene has been mapped to human chromosome 6 (6q24.1-25.2). Cytokine receptor Zcytor16 is a class II cytokine receptor and its binding to human IL-TIF could inhibit the proliferation and differentiation of hematopoietic cells. This invention also provide the test kit to detect genetic abnormality and cancer in patients.

L6 ANSWER 2 OF 7

ACCESSION NUMBER:

MEDLINE

DUPLICATE 1

DOCUMENT NUMBER:

2001286615

MEDLINE

21264727

PubMed ID: 11035029

TITLE:

Identification of the functional interleukin-22 (IL-22) receptor complex: the IL-10R2 chain (IL-10Rbeta) is a common chain of both the IL-10 and IL-22 (IL-10-related T cell-derived inducible factor, IL-TIF) receptor complexes.

AUTHOR:

Kotenko S V; Izotova L S; Mirochnitchenko O V; Esterova E; Dickensheets H; Donnelly R P; Pestka S

CORPORATE SOURCE:

Department of Molecular Genetics and Microbiology, Robert Wood Johnson Medical School, Piscataway, New Jersey 08854-5635, USA.. kotenkse@umdnj.edu

CONTRACT NUMBER:

1P30-CA72720 (NCI)

RO1-AI36450 (NIAID)

RO1-AI43369 (NIAID)

RO1-CA46465 (NCI)

SOURCE:

JOURNAL OF BIOLOGICAL CHEMISTRY, (2001 Jan 26) 276 (4) 2725-32.

PUB. COUNTRY:

Journal code: HIV; 2985121R. ISSN: 0021-9258.

LANGUAGE:

United States

FILE SEGMENT:

Journal; Article; (JOURNAL ARTICLE)

ENTRY MONTH:

English

ENTRY DATE:

Priority Journals

200106

Entered STN: 20010625

Last Updated on STN: 20010625

Entered Medline: 20010621

AB Interleukin-10 (IL-10)-related T cell-derived inducible factor (IL-TIF; provisionally designated IL-22) is a cytokine with limited homology to IL-10. We report here the identification of a functional IL-TIF receptor complex that consists of two receptor chains, the orphan CRF2-9 and IL-10R2, the second chain of the IL-10 receptor complex. Expression of the CRF2-9 chain in monkey COS cells renders them sensitive to IL-TIF. However, in hamster cells both chains, CRF2-9 and IL-10R2, must be expressed to assemble the functional IL-TIF receptor complex. The CRF2-9 chain (or the IL-TIF-R1 chain) is responsible for Stat recruitment. Substitution of the CRF2-9 intracellular domain with the IFN-gammaR1 intracellular domain changes the pattern of IL-TIF-induced Stat activation. The CRF2-9 gene is expressed in normal liver and kidney, suggesting a possible role for IL-TIF in regulating gene expression in these tissues. Each chain, CRF2-9 and IL-10R2, is capable of binding IL-TIF independently and can be cross-linked to the radiolabeled IL-TIF. However, binding of IL-TIF to the receptor complex is greater than binding to either receptor chain alone. Sharing of the common IL-10R2 chain between the IL-10 and IL-TIF receptor complexes is the first such case for receptor complexes with chains belonging to the class II cytokine receptor family, establishing a novel paradigm for IL-10-related ligands similar to the shared use of the gamma common chain (gamma(c)) by several cytokines, including IL-2, IL-4, IL-7, IL-9, and IL-15.

TI

... the IL-10R2 chain (IL-10Rbeta) is a common chain of both the IL-10 and IL-22 (IL-10-related T cell-derived inducible factor, IL-TIF) receptor complexes.

AB Interleukin-10 (IL-10)-related T cell-derived inducible factor (IL-TIF; provisionally designated IL-22) is a cytokine with limited homology to IL-10. We report here the identification of a functional IL-TIF receptor complex that consists of two receptor chains, the orphan CRF2-9 and IL-10R2, the second chain of the IL-10 receptor complex. Expression of the CRF2-9 chain in monkey COS cells renders them sensitive to IL-TIF. However, in hamster cells both chains, CRF2-9 and IL-10R2, must be expressed to assemble the functional IL-TIF receptor complex. The CRF2-9 chain (or the IL-TIF-R1 chain) is responsible for Stat recruitment. Substitution of the CRF2-9 intracellular domain with the IFN-gammaR1 intracellular domain changes the pattern of IL-TIF-induced Stat activation. The CRF2-9 gene is expressed in normal liver and kidney, suggesting a possible role for IL-TIF in regulating gene expression in these tissues. Each chain, CRF2-9 and IL-10R2, is capable of binding IL-TIF independently and can be cross-linked to the radiolabeled IL-TIF. However, binding of IL-TIF to the receptor complex is greater than binding to either receptor chain alone. Sharing of the common IL-10R2 chain between the IL-10 and IL-TIF receptor complexes is the first such case for receptor complexes with chains belonging to the class II cytokine receptor family.

CN 0 (Cross-Linking Reagents); 0 (Cytokines); 0 (IL-10-related T cell-derived inducible factor, IL-TIF); 0 (Interleukins); 0 (Ligands); 0 (Receptors, Interleukin); 0 (interleukin-10 receptor); 0 (interleukin-22); 0 (interleukin-22 receptor)

L6 ANSWER 3 OF 7

ACCESSION NUMBER:

BIOSIS COPYRIGHT 2001 BIOSIS

DOCUMENT NUMBER:

2001:264637 BIOSIS

TITLE:

PREV200100264637 Human IL-22 (IL-TIF) is a novel homolog of IL-10 that phosphorylates STAT 3 in colon carcinoma cells expressing the IL-22R1 chain.

AUTHOR(S):

Nagalakshmi, Marehalli L. (1); Parham, Christi (1); Rascle, Ann (1); Menon, Satish (1); Moore, Kevin (1); de Weal Malefyt, Rene (1)

CORPORATE SOURCE:

(1) DNAX Research Institute, 901 California Ave, Palo Alto, CA, 94304 USA

SOURCE:

FASEB Journal, (March 8, 2001) Vol. 15, No. 5, pp. A1052.

print.  
Meeting Info.: Annual Meeting of the Federation of American  
Societies for Experimental Biology on Experimental Biology  
2001 Orlando, Florida, USA March 31-April 04, 2001  
ISSN: 0892-6638.

DOCUMENT TYPE: Conference  
LANGUAGE: English  
SUMMARY LANGUAGE: English

AB DNA database mining and bioinformatics have revealed the existence of several novel proteins that have 'IL-10 like' structural motifs. Human IL-22 is one such protein has been described as a hepatocyte stimulatory factor inducing the production of acute phase proteins from hepatocytes. IL-22 binds to its specific receptor comprising the IL-22 R1 and the IL-10R2 (CRF2-4) chains. This interaction leads to the activation of signal transducer and activator of transcription factors (STATs-1 and -3). Quantitative PCR analysis (TaqMan) showed that human IL-22 mRNA is expressed in activated T cell cDNA libraries. The IL-22R1 chain mRNA is highly upregulated in normal and diseased colon cell libraries. Expression of this receptor chain was at very low levels in resting and activated monocyte, T, B and dendritic cell cDNA libraries. The second receptor component, the IL-10R2 chain is known to be expressed ubiquitously. In addition, we have shown that human IL-22 obtained from transient transfections activates STAT-3 in a colon carcinoma cell line, Colo205. Unstimulated cells expressed levels of IL-22R1 chain mRNA comparable to the human hepatoma cell line, HepG2. Levels of mRNA of the acute phase proteins - serum amyloid A, alpha - Antichymotrypsin and Haptoglobin were upregulated in IL-22 treated Colo205 cells. Future studies will be directed to identify the biological activities of this protein.

TI Human IL-22 (IL-TIF) is a novel homolog of IL-10 that phosphorylates STAT 3 in colon carcinoma cells expressing the IL-22R1 chain.

L6 ANSWER 4 OF 7 MEDLINE DUPLICATE 2  
ACCESSION NUMBER: 2000474382 MEDLINE  
DOCUMENT NUMBER: 20420346 PubMed ID: 10954742  
TITLE: Human interleukin-10-related T cell-derived inducible factor: molecular cloning and functional characterization as an hepatocyte-stimulating factor.  
AUTHOR: Dumoutier L; Van Roost E; Colau D; Renauld J C  
CORPORATE SOURCE: Ludwig Institute for Cancer Research, Brussels Branch and the Experimental Medicine Unit, Christian de Duve Institute of Cellular Pathology, Universite Catholique de Louvain, Avenue Hippocrate 74, B1200-Brussels, Belgium.  
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (2000 Aug 29) 97 (18) 10144-9. Journal code: PV3; 7505876. ISSN: 0027-8424.  
PUB. COUNTRY: United States  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
OTHER SOURCE: GENBANK-AJ277247  
ENTRY MONTH: 200010  
ENTRY DATE: Entered STN: 20001012  
Last Updated on STN: 20001012  
Entered Medline: 20001005

AB IL-10-related T cell-derived inducible factor (IL-TIF or IL-21) is a new cytokine structurally related to IL-10 and originally identified in the mouse as a gene induced by IL-9 in T cells and mast cells. Here, we report the cloning of the human IL-TIF cDNA, which shares 79% amino acid identity with mouse IL-TIF and 25% identity with human IL-10. Recombinant human IL-TIF was found to activate signal transducer and activator of transcription factors-1 and -3 in several hepatoma cell lines. IL-TIF stimulation of HepG2 human hepatoma cells up-regulated the production of acute phase reactants such as serum amyloid A, alpha1-antichymotrypsin, and haptoglobin. Although IL-10 and IL-TIF have distinct activities, antibodies directed against the beta chain of the IL-10 receptor blocked the induction of acute phase reactants by IL-TIF, indicating that this chain is a common component of the IL-10 and IL-TIF receptors. Similar acute phase reactant induction was observed in mouse liver upon IL-TIF injection, and IL-TIF expression was found to be rapidly increased after lipopolysaccharide (LPS) injection, suggesting that this cytokine contributes to the inflammatory response in vivo.

AB IL-10-related T cell-derived inducible factor (IL-TIF or IL-21) is a new cytokine structurally related to IL-10 and originally identified in the mouse as a gene induced by IL-9 in T cells and mast cells. Here, we report the cloning of the human IL-TIF cDNA, which shares 79% amino acid identity with mouse IL-TIF and 25% identity with human IL-10. Recombinant human IL-TIF was found to activate signal transducer and activator of transcription factors-1 and -3 in several hepatoma cell lines. IL-TIF stimulation of HepG2 human hepatoma cells up-regulated the production of acute phase reactants such as serum amyloid A, alpha1-antichymotrypsin, and haptoglobin. Although IL-10 and IL-TIF have distinct activities, antibodies directed against the beta chain of the IL-10 receptor blocked the induction of acute phase reactants by IL-TIF, indicating that this chain is a common component of the IL-10 and IL-TIF receptors. Similar acute phase reactant induction was observed in mouse liver upon IL-TIF injection, and IL-TIF expression was found to be rapidly increased after lipopolysaccharide (LPS) injection, suggesting that this cytokine contributes to the inflammatory response.

CN 0 (Acute-Phase Proteins); 0 (Cytokines); 0 (DNA, Complementary); 0 (IL-10-related T cell-derived inducible factor, IL-TIF); 0 (Recombinant Proteins); 0 (Trans-Activators)

L6 ANSWER 5 OF 7 MEDLINE DUPLICATE 3  
ACCESSION NUMBER: 2000126044 MEDLINE  
DOCUMENT NUMBER: 20126044 PubMed ID: 10657629  
TITLE: Cloning and characterization of IL-10-related T cell-derived inducible factor (IL-TIF), a novel cytokine structurally related to IL-10 and inducible by IL-9.  
AUTHOR: Dumoutier L; Louahed J; Renauld J C  
CORPORATE SOURCE: Ludwig Institute for Cancer Research, Brussels, Belgium.  
SOURCE: JOURNAL OF IMMUNOLOGY, (2000 Feb 15) 164 (4) 1814-9. Journal code: IJB; 2985117R. ISSN: 0022-1767.  
PUB. COUNTRY: United States  
LANGUAGE: English  
Journal; Article; (JOURNAL ARTICLE)

FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals  
OTHER SOURCE: GENBANK-AJ249491; GENBANK-AJ249492  
ENTRY MONTH: 200003  
ENTRY DATE: Entered STN: 20000320  
Last Updated on STN: 20000320  
Entered Medline: 20000309

AB IL-9 is a Th2 cytokine active on various cell types such as T and B lymphocytes, mast cells, and eosinophils, and potentially involved in allergy and asthma. To understand better the molecular mechanisms underlying the activity of this cytokine, we used a cDNA subtraction method to identify genes specifically induced by IL-9 in mouse T cells. One of the IL-9-regulated genes isolated by this approach turned out to encode a 180-amino acid long protein, including a potential signal peptide, and showing 22% amino acid identity with IL-10. This protein, designated IL-10-related T cell-derived inducible factor (IL-TIF), is induced by IL-9 in thymic lymphomas, T cells, and mast cells, and by lectins in freshly isolated splenocytes. Experiments concerning the mechanism regulating IL-TIF expression in T cells indicate that IL-9 induction is rapid (within 1 h), does not require protein synthesis, and depends on the activation of the Janus kinase (JAK)-STAT pathway. In vivo, constitutive expression of IL-TIF was detected by RT-PCR in thymus and brain, suggesting that the role of this new factor is not restricted to the immune system. Transfection of HEK293 cells with the IL-TIF cDNA resulted in the production of a glycosylated protein of about 25 kDa that was found to induce STAT activation in mesangial and neuronal cell lines. Further studies will have to address the possibility that some of the IL-9 activities may be mediated by IL-TIF.

TI Cloning and characterization of IL-10-related T cell-derived inducible factor (IL-TIF), a novel cytokine structurally related to IL-10 and inducible by IL-9.

AB . . . a potential signal peptide, and showing 22% amino acid identity with IL-10. This protein, designated IL-10-related T cell-derived inducible factor (IL-TIF), is induced by IL-9 in thymic lymphomas, T cells, and mast cells, and by lectins in freshly isolated splenocytes. Experiments concerning the mechanism regulating IL-TIF expression in T cells indicate that IL-9 induction is rapid (within 1 h), does not require protein synthesis, and depends on the activation of the Janus kinase (JAK)-STAT pathway. In vivo, constitutive expression of IL-TIF was detected by RT-PCR in thymus and brain, suggesting that the role of this new factor is not restricted to the immune system. Transfection of HEK293 cells with the IL-TIF cDNA resulted in the production of a glycosylated protein of about 25 kDa that was found to induce STAT activation. . . cell lines. Further studies will have to address the possibility that some of the IL-9 activities may be mediated by IL-TIF.

CN 0 (Cytokines); 0 (IL-10-related T cell-derived inducible factor, IL-TIF); 0 (Interleukin-9); 0 (RNA, Messenger)

L6 ANSWER 6 OF 7 MEDLINE DUPLICATE 4  
ACCESSION NUMBER: 2001223439 MEDLINE  
DOCUMENT NUMBER: 21069354 PubMed ID: 11197690  
TITLE: IL-TIF/IL-22: genomic organization and mapping of the human and mouse genes.  
AUTHOR: Dumoutier L; Van Roost E; Ameye G; Michaux L; Renauld J C  
CORPORATE SOURCE: Ludwig Institute for Cancer Research, Brussels Branch, Experimental Medicine Unit, Christian de Duve Institute of Cellular Pathology, Brussels, Belgium.  
SOURCE: GENES AND IMMUNITY, (2000 Dec) 1 (8) 488-94.  
PUB. COUNTRY: Journal code: DXO; 100953417. ISSN: 1466-4879.  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200104  
ENTRY DATE: Entered STN: 20010502  
Last Updated on STN: 20010502  
Entered Medline: 20010426

AB IL-TIF is a new cytokine originally identified as a gene induced by IL-9 in murine T lymphocytes, and showing 22% amino acid identity with IL-10. Here, we report the sequence and organization of the mouse and human IL-TIF genes, which both consist of 6 exons spreading over approximately 6 Kb. The IL-TIF gene is a single copy gene in humans, and is located on chromosome 12q15, at 90 Kb from the IFN gamma gene, and at 27 Kb from the AK155 gene, which codes for another IL-10-related cytokine. In the mouse, the IL-TIF gene is located on chromosome 10, also in the same region as the IFN gamma gene. Although it is a single copy gene in BALB/c and DBA/2 mice, the IL-TIF gene is duplicated in other strains such as C57Bl/6, FVB and 129. The two copies, which show 98% nucleotide identity in the coding region, were named IL-TIF alpha and IL-TIF beta. Beside single nucleotide variations, they differ by a 658 nucleotide deletion in IL-TIF beta, including the first non-coding exon and 603 nucleotides from the promoter. A DNA fragment corresponding to this deletion was sufficient to confer IL-9-regulated expression of a luciferase reporter plasmid, suggesting that the IL-TIF beta gene is either differentially regulated, or not expressed at all.

TI IL-TIF/IL-22: genomic organization and mapping of the human and mouse genes.

AB IL-TIF is a new cytokine originally identified as a gene induced by IL-9 in murine T lymphocytes, and showing 22% amino acid identity with IL-10. Here, we report the sequence and organization of the mouse and human IL-TIF genes, which both consist of 6 exons spreading over approximately 6 Kb. The IL-TIF gene is a single copy gene in humans, and is located on chromosome 12q15, at 90 Kb from the IFN . . . gamma gene, and at 27 Kb from the AK155 gene, which codes for another IL-10-related cytokine. In the mouse, the IL-TIF gene is located on chromosome 10, also in the same region as the IFN gamma gene. Although it is a single copy gene in BALB/c and DBA/2 mice, the IL-TIF gene is duplicated in other strains such as C57Bl/6, FVB and 129. The two copies, which show 98% nucleotide identity in the coding region, were named IL-TIF alpha and IL-TIF beta. Beside single nucleotide variations, they differ by a 658 nucleotide deletion in IL-TIF beta, including the first non-coding exon and 603 nucleotides from the promoter. A DNA fragment corresponding to this deletion was sufficient to confer IL-9-regulated expression of a luciferase reporter plasmid, suggesting that the IL-TIF beta gene is either differentially regulated, or not expressed at all.

CN 0 (Cytokines); 0 (IL-10-related T cell-derived inducible factor, IL-TIF); 0 (Interleukins); 0 (interleukin-22)

L6 ANSWER 7 OF 7 BIOSIS COPYRIGHT 2001 B  
 ACCESSION NUMBER: 2000:468282 BIOSIS  
 DOCUMENT NUMBER: PREV200000468282  
 TITLE: IL-TIF induces acute phase reactant  
 production by hepatocytes through IL-10Rbeta.  
 AUTHOR(S): Dumoutier, L. (1); Van Roost, E. (1); Colau, D. (1);  
 Renaud, J.-C. (1)  
 CORPORATE SOURCE: (1) Brussels Branch, Ludwig Institute for Cancer Research,  
 Brussels Belgium  
 SOURCE: Immunology Letters, (September, 2000) Vol. 73, No. 2-3, pp.  
 261. print.  
 Meeting Info.: 24th European Immunology Meeting of the  
 European Federation of Immunological Societies (EFIS)  
 Poznan, Poland September 23-26, 2000 European Federation of  
 Immunological Societies  
 ISSN: 0165-2478.

DOCUMENT TYPE: Conference  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English

TI IL-TIF induces acute phase reactant production by  
 hepatocytes through IL-10Rbeta.

IT . . .  
 inflammatory bowel disease: digestive system disease

IT Chemicals & Biochemicals  
 IL-10 receptor beta [interleukin 10 receptor beta]; IL-9 [interleukin  
 9]; IL-TIF receptor [interleukin TIF-receptor]; LPS  
 [lipopolysaccharide]; toxin; STAT-1: activation; al-antichymotrypsin;  
 acute phase reactant, production; amyloid A: acute phase reactant,  
 production, serum; haptoglobin: acute phase reactant, production; human  
 IL-10 [human interleukin-10]; human IL-TIF [human  
 interleukin TIF]: expression; human IL-TIF cDNA  
 [human interleukin TIF complementary DNA]; mouse IL-  
 TIF [mouse interleukin IL-TIF]; recombinant  
 human IL-TIF; transcription factors: activation;  
 human IFNg gene (Hominidae); human IL-TIF gene  
 (Hominidae): exons, introns, localization

IT Alternate Indexing  
 Asthma (MeSH); Inflammatory Bowel Diseases (MeSH)

=> end

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L1: Entry 1 of 1

File: DWPI

Jun 7, 2001

DERWENT-ACC-NO: 2001-356158

DERWENT-WEEK: 200137

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TITLE: New soluble cytokine receptor polypeptides and polynucleotides, useful for diagnosing and treating cancer and inflammatory conditions

## ABTX:

(a) an aa sequence at least 90% identical to aa residues 22-231 or 22-210 of S1, where the polypeptide binds IL-TIF (undefined) or antagonizes IL-TIF activity; or

## ABTX:

(16) an isolated soluble cytokine receptor polypeptide (XIII) comprising an aa sequence at least 90% identical to a sequence of aa residues 22-231 or 22-210 of S1, where (XIII) binds IL-TIF (undefined) or antagonizes IL-TIF activity;

## ABTX:

MECHANISM OF ACTION - IL-TIF antagonist.

## ABTX:

(1) inhibiting IL-TIF induced proliferation or differentiation of hematopoietic cell(s) (progenitors);

## ABTX:

(2) reducing IL-TIF induced or IL-9 induced inflammation; and

## ABTX:

A polynucleotide comprising at least 14 contiguous nucleotides of S1 or its complement is useful for detecting a genetic abnormality and cancer in a patient (all claimed). Heteromeric/multimeric receptor polypeptides such as soluble zcytor 16/CRF2-4 can be used to reduce progression and symptoms of cancer. Zcytor16 polypeptides can also be used to detect IL-TIF levels which is indicative of pathological conditions including inflammatory states (e.g. rheumatoid arthritis) and cancer. Antibodies that bind zcytor16 polypeptides and the polypeptides themselves are useful for the treatment of inflammation, inflammatory diseases (e.g. infection, asthma, inflammatory bowel disease, rheumatoid arthritis and atherosclerosis) and autoimmune diseases.

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L1: Entry 1 of 1

File: DWPI

Jun 7, 2001

DERWENT-ACC-NO: 2001-356158

DERWENT-WEEK: 200137

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TITLE: New soluble cytokine receptor polypeptides and polynucleotides, useful for diagnosing and treating cancer and inflammatory conditions

INVENTOR: CHEN, Z; KINDSVOGEL, W ; PRESNELL, S R ; XU, W

PRIORITY-DATA: 2000US-0244610 (October 31, 2000), 1999US-0169049 (December 3, 1999), 2000US-0232219 (September 13, 2000)

## PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
WO 200140467 A1	June 7, 2001	E	184	C12N015/12

INT-CL (IPC): A61K 38/17; C07K 14/715; C07K 16/28; C12N 5/10; C12N 15/12; C12N 15/62; C12Q 1/68

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